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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,380	09/22/2000	Gregory Donoho	LEX-0042-USA	9804

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/03/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/667,380	GREGORY DONOHO	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

Applicants' amendment and response to office action dated October 1, 2002, filed on March 7, 2003 in paper #14 is acknowledged. Claims 1 and 2 have been amended. New claims 4 and 5 have been added. Therefore, claims 1-5 are currently pending and are under examination.

Response to Remarks and arguments

Oath or Declaration

Objection to defective oath or declaration is withdrawn in view of Applicants' submission of a supplemental declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date.

Claim 3

The error concerning claim 3 rejection in the previous office action is noted and is corrected in this office action (please see rejection under 101).

Rejections under 35 USC § 112, First Paragraph

The rejection of claim 1under 35 U.S.C. 112, first paragraph is withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Rejection of claims 1 and 2 under 35 U.S.C. 112, second paragraph, is withdrawn in view of Applicants' amendment to claims 1 and 2.

Rejections under 35 U.S.C. § 102

Rejection of claim 1 under 35 U.S.C. 102 is withdrawn in view of Applicants' amendment to claim 1.

New grounds of Rejection

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title"

Claims 1-5 are rejected under 35 U.S.C. 101 because the specification does not provide either a specific or substantial asserted utility or a well-established utility, and thus, does not support the claimed invention. The claimed proteins are not supported by either a specific asserted utility or a well established utility because the specification fails to assert any utility for the claimed proteins or the polynucleotides encoding these proteins and neither the specification as filed nor any art of record disclose or suggest any activity for the claimed proteins or the polynucleotides encoding them such that another non-asserted utility would be well established. Note, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be assessed.

The specification indicates (see page 2-7), that the novel human proteins (NHP), share structural similarity with animal trypsin inhibitor proteins. Additionally the invention contemplates a nucleotide sequence encoding a contiguous NHP open reading frame (ORF), however specification fails to provide any description of the NHP, which has an activity of the trypsin inhibitor protein. Applicants assert (page 2, lines 2-6) that the NHPs described for the first time herein share structural similarity with animal trypsin inhibitor proteins. Also as such the novel genes represent a new class of proteins with a range of homologues and orthologs that transcend phyla and a range of species. Specification has not provided any percentage similarity of claimed NHPs with any trypsin inhibitor protein or has described or demonstrated a correlation of this structural homology with any function that trypsin inhibitor protein may have. By asserting a protein sharing structural similarity with animal trypsin inhibitor proteins it is intended proteins exhibiting activity similar, but not necessarily identical, to an activity of the animal trypsin inhibitor protein. The specification has not provided any sequence identity of NHPs or percent similarity to the sequence of known member of trypsin inhibitor protein or to the sequence of a member that represents a new class of protein as stated at page 2, lines 4-5. No

activity of the claimed protein has been provided in the specification that can be correlated with trypsin inhibitor protein or with the activity of a new class of protein.

A sequence identity search for SEQ ID NO: 1 using GenBank database indicates the alignments and percent similarity to sequences, identified as Accession NOs: AAS60871 (Lillie et al.) and AAD17766 (Vernet et al.). Lillie et al. (US 2002/0110815 A1, August 15, 2002, page 1, col 2) teach a human cancer agent-resistance marker #530, which has 99.8% sequence identity to SEQ ID NO: 1 (see sequence alignment result, N_Geneseq_032802, Accession NO: AAS60871, January 29, 2002), while Vernet et al. (WO 01/62928 A2, August 30, 2001) teach a human novel trypsin inhibitor-like protein, NOV-4b and NOV-4d (see page 1, Table 1, page 82, 83, 87 and 88), wherein DNA encoding NOV-4D is having 98.9% sequence identity to SEQ ID NO: 1 (see sequence alignment result, N_Geneseq_032802, Accession NO: AAD17766, December 10, 2001).

A sequence identity search for SEQ ID NO: 2 using GenBank database indicates the alignments and percent similarity to sequences, identified as Accession NOs: Q9H0B8 (Wambutt et al.) and AAE10616 (Vernet et al.). Wambutt et al. teach a human hypothetical 55.9 kDA protein, which has 99.9% sequence identity to SEQ ID NO: 2 (see sequence alignment result, SPTREMBL_19, Accession NO: Q9H0B8, March 1, 2001), while Vernet et al. (WO 01/62928 A2, August 30, 2001) teach a human novel trypsin inhibitor-like protein, NOV-4b and NOV-4d (see page 1, Table 1, page 82, 83, 87 and 88), wherein protein NOV-4B is having 99.4% sequence identity to SEQ ID NO: 2 (see sequence alignment result, A-Geneseq_032802, Accession NO: AAE10616, December 10, 2001).

Thus, the foregoing indicates that the sequence of SEQ ID NO: 1 and 2 of the instant application have a lower percent similarity (98.9 and 99.4% respectively) to the nucleic acid and protein sequence of Vernet's trypsin inhibitor-like protein, while the instant sequence of SEQ ID NO: 1 and 2 demonstrate a relatively higher percent similarity (99.8% and 99.9% respectively) to the nucleic acid and protein sequence of Lillie's cancer agent-resistance marker and Wambutt's hypothetical protein respectively. Lillie's markers can be used to determine the sensitivity or resistance of cancer cells to a therapeutic agent, furthermore the markers can be used in selecting

appropriate treatment agents (please see page 1, col 1 to col 2, paragraph 0006). Lillie's cancer agent resistance-marker or the selected therapeutic agent using these markers do not describe any activity of trypsin inhibitor-like protein. Therefore, one of skill in the art would question that the protein has been placed in the correct family of protein i.e. trypsin inhibitor-like protein as is asserted. The search result indicates that the claimed protein more likely belongs to a family other than that asserted i.e. a cancer agent-resistance marker. The specification fails to disclose any property and biological activity of NHPs which share the specified activities of trypsin inhibitor-like protein. The artisan would need to prepare, isolate and analyze the protein in order to determine its function and use, thus the utility is not substantial. Therefore, only on the basis of sequence similarity it cannot be interpreted that NHPs protein would have similar activities of trypsin inhibitor-like protein family proteins. The utility cannot be extrapolated from family.

Based on the specification (pages 2-7), any biological activity of the nucleic acid and encoded polypeptide itself has not been provided. However, generalized statements regarding uses have been provided on pages 2-13 of the specification, but are discussed in the context of being used for further research, but to do what? The function/biological activity of the protein is not per se set forth in the instant specification. One skilled in the art should not have to engage in discovering genomics to learn how to use the invention. Therefore, the utility of NHPs encoded by a nucleic acid that shares structural similarity with animal trypsin inhibitor proteins is not a substantial utility because there is no real world context in which to use a protein having no known activity. This situation requires carrying out future additional research to identify or reasonably confirm a "real world" context of use and therefore do not define specific and substantial utility.

Other activities that the protein may exhibit are listed throughout pages 8-15 of the specification. The specification at page 8 indicates that suitably labeled NHP nucleotide probes can be used to screen a human genomic library, the identification and characterization of human genomic clones is helpful for identifying polymorphisms, determining the genomic structure of a given locus/allele and designing diagnostic tests. Also, the specification describes at page 11-12 that NHPs or NHP peptides, NHP nucleotide sequences can be useful for the detection of mutant NHPs or inappropriately expressed NHPs for the diagnosis of disease. Further, the specification

asserts that the NHP proteins or peptides, NHP fusion proteins, NHP nucleotide sequences, host cell expression system and genetically engineered cells and animals can be used for screening for drugs (or high throughput screening of combinatorial libraries) effective in the treatment of the symptomatic or phenotypic manifestations of perturbing the normal function of NHP in the body. There are no teachings provided in regards to identifying polymorphisms or use of inappropriately expressed NHPs for the diagnosis of diseases or use of genetically engineered cells for drug screening. At page 13, lines 12-15 specification indicates that in addition to the genes encoding trypsin inhibitors, the described NHPs share significant similarity to a variety of cancer pathogenesis proteins, sperm glycoproteins, and secretory proteins. However, the specification fails to provide any activity of NHPs that can be correlated with the activity of these proteins. Therefore, these utilities are not substantial utilities because there is no real world context to use these polynucleotides and polypeptides without further research to confirm this utility. The utilization of NHP genes and its product in gene therapy and other therapeutics have been described in pages 12-13. However, generalized statements regarding the activity of the gene product are set forth at pages 12-13. In summary, the polypeptides claimed do not have a credible, specific or well-established or even demonstrable utility and therefore lacks utility under 35 U.S.C. 101.

In the instant case, the failure of the specification to specifically identify why the claimed invention is believed to be useful renders the claimed invention deficient under 35 USC 101. No specific biological activity has been identified for the protein set forth in SEQ ID NO: 2 or for the polynucleotides of SEQ ID NO: 1 encoding the protein other than the fact that the protein may have a similar activity of trypsin inhibitor-like protein (p. 2). The person having ordinary skill in the art would not be able to identify any specific activity for the protein comprising or related to SEQ ID NO: 2 based on its structure alone for the reasons set forth above. General statements that a composition has an unspecified biological activity or that do not explain why a composition with that activity is believed to be useful fails to set forth a "specific utility." Brenner v. Manson, 383 US 519, 148 USPQ 689 (Sup. Ct.1966) (general assertion of similarities to known compounds known to be useful without sufficient corresponding explanation why claimed compounds are believed to be similarly useful is insufficient under 35 USC 101).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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May 26, 2003